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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/927,436	08/13/2001	Mitra Tadayoni-Rebek	0942.5300001/RWE/AGU	6227

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STERNE, KESSLER, GOLDSTEIN & FOX PLLC
1100 NEW YORK AVENUE, N.W.
WASHINGTON, DC 20005

EXAMINER	
LUKTON, DAVID	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 01/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/927,436	TADAYONI-REBEK ET AL.	
	Examiner	Art Unit	
	David Lukton	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-38* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

G1: Segment A is a labeled peptide that contains 10-30 amino acids;

G2: Segment A can be whatever the claims permit, provided that G1 is excluded;

G3: Segment A is labeled with a fluorescent group selected from fluorescein, carboxyfluorescein, fluorescein isothiocyanate, JOE, rhodamine, TAMTA or TMR;

G4: Segment A can be labeled with any "label" that is permitted by the claims, provided that G3 is excluded;

G5: segment B is a protein;

G6: segment B is a nucleic acid;

G7: integer variable "n" is limited to a range of 1 – 9;

G8: integer variable "n" is limited to a range of 10-19;

G9: integer variable "n" is limited to a range of 20-29;

G10: integer variable "n" is limited to a range of 30-39;

G11: integer variable "n" is limited to a range of 40-49;

G12: integer variable "n" is limited to a range of 50-100.

Restriction to one of the following inventions is required under 35 U.S.C. §121:

1. Claims 1-10, drawn to a "marker molecule", limited to G1, G3 and G5.

2. Claims 1-7 and 10, drawn to a "marker molecule", limited to G2, G3 and G5.

3. Claims 1-10, drawn to a "marker molecule", limited to G1, G4 and G5.

4. Claims 1-7 and 10, drawn to a "marker molecule", limited to G2, G4 and G5.

5. Claims 1-10, drawn to a "marker molecule", limited to G6.

6. Claims 11-12, drawn to a composition comprising two or more molecules of Group 1.

7. Claims 11-12, drawn to a composition comprising two or more molecules of Group 2.

8. Claims 11-12, drawn to a composition comprising two or more molecules of Group 3.

9. Claims 11-12, drawn to a composition comprising two or more molecules of Group 4.

10. Claims 11-12, drawn to a composition comprising two or more molecules of Group 5.

11. Claims 13-15, drawn to a method, limited to G5.

12. Claims 13-15, drawn to a method, limited to G6.

13. Claims 16-20, drawn to a method of preparing a marker molecule.

14. Claims 21-23, drawn to a method of labeling a marker molecule.

15. Claims 24 and 26, drawn to a method of electrophoresis.

16. Claim 25, drawn to a method of characterizing molecules.

17. Claim 27, drawn to a peptide, limited to G7.

18. Claim 27, 29-33, drawn to a peptide, limited to G8

19. Claim 27, drawn to a peptide, limited to G9.

20. Claim 27, drawn to a peptide, limited to G10.

21. Claim 27, drawn to a peptide, limited to G11.

22. Claim 27, drawn to a labeled peptide, limited to G12.

23. Claim 28, drawn to a labeled peptide, limited to G7.

24. Claim 28, drawn to a labeled peptide, limited to G8

25. Claim 28, drawn to a labeled peptide, limited to G9.

26. Claim 28, drawn to a labeled peptide, limited to G10.

27. Claim 28, drawn to a labeled peptide, limited to G11.

28. Claim 28, drawn to a labeled peptide, limited to G12.

29. Claims 34-35, drawn to a "tagged" peptide, limited to G7.

30. Claims 34-35, drawn to a "tagged"peptide, limited to G8

31. Claims 34-35, drawn to a "tagged"peptide, limited to G9.

32. Claims 34-35, drawn to a "tagged"peptide, limited to G10.

33. Claims 34-35, drawn to a "tagged" peptide, limited to G11.

34. Claims 36-38, drawn to a kit.

The claimed inventions are distinct.

Claim 1 has been sequestered into five different groups. To begin with, claim 1 encompasses almost any peptide or protein. The term "label" is not effective to impose any limitation. Consider, for example the following simple peptide:

Gly-His-Ala-Phe-Arg.

One could argue that this is really the peptide HAFR which has been "labelled" with glycine, or the peptide GHAF which has been "labelled" with arginine. But even if the limitations of claim 3 were introduced into claim 1, there would still be tens of thousands of references which would form the basis for a valid §103 rejection. As acknowledged by applicants (page 5, last two lines), tryptophan and tyrosine absorb in the UV. Phenylalanine also absorbs in the UV. What appears not to be stated in the specification is that tryptophan is also fluorescent (though weakly). Thus, any peptide or protein which contains a tryptophan, phenylalanine or tyrosine would be encompassed by claim 1. For similar reasons, claim 1 encompasses any polynucleotide. But even if claim 1 were amended to require that the molecule had to be labelled with fluorescein or rhodamine (only), there would still be a large number of references which would anticipate, or render obvious claim 1. If a given reference were to disclose that a "first" peptide or protein binds to a "second" protein, or to a tissue or cell type, then there would be motivation to attach a fluorescein or rhodamine group to that "first" peptide or protein. If a given reference were to disclose that a given peptide or protein

is cleaved by a given protease, there is motivation to attach a fluorescein or rhodamine group to the peptide or protein. Thus, the possibilities are limitless, even before considering the issue of polynucleotides, and even without considering radiolabels.

Groups {1-5} and {6-10} are related as combination/subcombination. The compounds of claim 1 can be used as such, without the presence of other like molecules. However, in the event that one of Groups 1-5 is elected, and claims found allowable, the possibility of rejoining claims 11-12 would be considered, provided that whatever limitations have been introduced into claim 1 are also introduced into claims 11-12.

Groups 11 and 12 are distinct. Group 11 encompasses primarily peptides and proteins (although hybrid molecules such as polysaccharide/protein conjugates would also be included). Group 12 encompasses primarily polynucleotides. Clearly, methods of separating proteins and polynucleotides are distinct (notwithstanding the fact that at some theoretical level there are commonalities between the two methods).

Claim 27 has been sequestered into five different groups. To search for, and reject over, every known sequence that conforms to the genus of claim 27 would constitute an "undue burden" even for ten different examiners. In the online "registry" file, there are 50,000 known peptides that have a sequence length of 4 – 100 amino acids, and which have a cysteine residue as the N-terminal amino acid (not all of the references were published before 8/11/00). If the sequence length were limited to a range of 10-20 amino acids, there

would still be more than 15,000 known sequences. And even if claim 27 were amended so that there could be no more and no less than 10 amino acids, there would still be more than 2800 known sequences that would fall within the scope of the genus. Following are examples of known (in the literature) decapeptides bearing a cysteine at the N-terminus:

CPGCGCPGCN
CGPCGCGPCN
CYFDDSSNWC
CSNKLHFAFR
CHFEATYLEL
CVEFATYLEL
CLHEFHRNCV
CYSNSQPVWL
CSDTILKESI
CDSPPLFKLS

The situation is little improved for the case of claim 28; as indicated above, the requirements of claim 28 are met if (in addition to an N-terminal cysteine), there is at least one Phe, Tyr or Trp residue. In fact, the universe of peptides meeting the limitations of claim 28 is potentially far greater than those which meet the limitations of claim 27. Consider, for example the following two peptides:

CVEFATYLEL

WRSACVEFATYLEL

The first of these is a known peptide, and falls within the scope of claim 27. The second of these is obtained by adding the tetrapeptide WRSA to the N-terminus of the

first peptide. The tetrapeptide WRSA contains an indole group which is both fluorescent, and UV-absorbing. Accordingly, the peptide **WRSA**CVEFATYLEL meets the limitations of claim 28. One of the points is that claim 28 does not actually require that a cysteine be present at the N-terminus; accordingly, the universe of peptides that would meet the limitations of claim 28 is far greater than that which meets the limitations of claim 27. Even if claim 27 were amended to require that "n" could be no more and no less than 8, and that there must be a fluorescein or a rhodamine bonded somewhere to the peptide, there would still be a very large number of references that would render the claim obvious.

Group 34 is distinguished from Groups 1-5 in that Group 34 requires a container and instructions, which are not required by Groups 1-5. However, in the event that any of Groups 1-5 is elected, and claims therein found allowable, the "kit" claims will be rejoined therewith for further examination. Of course, any limitations introduced into the Group 1-5 claims would have to be introduced into the "kit" claims prior to rejoining. Similarly, in the event that any of Groups 1-5 is elected, and claims therein found allowable, claims drawn to a method of making or using the "marker molecules" will be rejoined for further examination (with introduction of the same limitations, of course). The same holds for the composition claims (Groups 6-10).

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their divergent subject matter, restriction for examination purposes as indicated is proper.

Applicant is reminded that upon cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently filed petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(h).

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

* * * * *

In addition to the foregoing, applicants are required under 35 U.S.C. §121 to elect disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

In the event that one of Groups 1-5 is chosen for initial examination, the species to be elected are as follows:

(a) a specific "segment A", including an identification of the "label", and the specific location (or multiple locations) in the molecule where the label is bonded.

(b) a specific L; a statement that "L" is a bond will be taken as a statement that "L" is a covalent bond (as opposed to some sort of functional group)

(c) a "segment B", identified with as much specificity as the specification permits. For example, segment B might be a protein of 6,000 Daltons or a deoxyribonucleic acid consisting of 2000 deoxyribose units.

(d) an isoelectric point of the marker molecule.

. . . .

In the event that one of Groups 6-10 is chosen for initial examination, identification of two different "marker molecules" that are present in the mixture is required. Each of these molecules is identified in the same way that the molecule of Groups 1-5 is identified, i.e., the four species indicated above.

. . . .

In the event that one of Groups 11-12 is chosen for initial examination, identification of a single "marker molecule" that is present in the mixture is required. This molecule is identified in the same way that the molecule of Groups 1-5 is identified, i.e., the four species indicated above. An additional election required is that of a method of separation; this is not specified in the case of claim 14. The method might be electrophoresis or isoelectric focusing or one of the other methods recited, e.g., at page 24, paragraph 0069.

. . . .

In the event that Group 13 is chosen for initial examination, identification of a specific "marker molecule" that is the "target" of the synthesis is required. An additional specie to be elected is that of a "molecule" as recited in step (a) of claims 16 and 19, and a specific "label" that is to be used for the "labeling" step.

. . . .

In the event that Group 14 is chosen for initial examination, identification of a specific labeled "marker molecule" that is the "target" of the synthesis is required. Thus, it should be clear what the "protein" of step (e), claim 21 is, as well as what the "label" is, as well as the number of "labels" present, as well as the point(s) of attachment of the label.

. . . .

In the event that Group 15 is chosen for initial examination, identification of a single "marker molecule" that is present in the mixture is required. This molecule is identified in the same way that the molecule of Groups 1-5 is identified, i.e., the four species indicated above.

. . . .

In the event that Group 16 is chosen for initial examination, identification of a single "marker molecule" that is present in the mixture is required. This molecule is

identified in the same way that the molecule of Groups 1-5 is identified, i.e., the four species indicated above. An additional election required is that of a method of separation. The method might be electrophoresis or isoelectric focusing or one of the other methods recited, e.g., at page 24, paragraph 0069.

. . . .

In the event that one of Groups 17-22 is chosen for initial examination, identification of a specific peptide is required.

. . . .

In the event that one of Groups 23-28 is chosen for initial examination, identification of a specific peptide is required. In addition, identification of a specific chromophore, fluorophore, or UV absorbing group is required, along with the number of such groups that are present, and the point(s) of attachment.

. . . .

In the event that one of Groups 29-33 is chosen for initial examination, identification of a specific peptide is required. In addition, identification of a specific "tag" moiety is required, along with the number of such moieties that are present, and the point(s) of attachment to the peptide.

. . . .

In the event that Group 34 is chosen for initial examination, the species to be elected

are as follows:

(d) a specific "segment A", including an identification of the "label", and the specific location (or multiple locations) in the molecule where the label is bonded.

(e) a specific L; a statement that "L" is a bond will be taken as a statement that "L" is a covalent bond (as opposed to some sort of functional group)

(f) a "segment B", identified with as much specificity as the specification permits. For example, segment B might be a protein of 6,000 Daltons or a deoxyribonucleic acid consisting of 2000 deoxyribose units.

(d) the isoelectric point of the marker molecule.

Applicant is advised that a response to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a generic claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are witten in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP 809.02(a).

Should applicant traverse on the ground that the species are not patentable distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. §103 of the other invention.

✷

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached at 571-272-0951.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

DAVID LUKTON
PATENT EXAMINER
GROUP 1600